Pneumonic pasteurellosis is a common disease of respiratory system of cattle as result of inflammation of pulmonary parenchyma which is usually accompanied by inflammation of bronchioles and often by pleurisy. It is a disease of great economic importance, particularly in North America and Britain where it has caused great loss since before 1990s. The disease in its typical clinical form, is highly infectious, often fatal and with very serious economic impact in animal industry. *Mannheimia haemolytica* biotype A serotype1 is the most common cause of pneumonia. Eleven serotypes have been demonstrated within *M.haemolytica*, Serotypes 6, 2, 9 and 11 and untypable serotypes have been found in lesions of Pneumonic Pasteurellosis (Angen *et al*., 2002). Several respiratory viruses including PI-3 virus, BHV-1 and BRSV may predispose the bacterial incubation (Quinn *et al*., 2002). An acute fatal respiratory disease was also induced in cattle by previous infection BHV-1 challenged with *M.haemolytica* (Hodgson *et al*., 2005).

Clinical signs of respiratory distress usually develop within 10 to 14 days, in adult animals after being exposed to stress (Radostits *et al*., 2000). Infected animals appear extremely dull with reduced appetite, depression, bronchopneumonia, abnormal lung sound, coughing, mucoid to mucopurulent nasal discharge, high fever (40-41^{o}C or 104-106^{o}F) (Ackermann and Brogden,2000).

It is well established that Pneumonic Pasteurellosis is responsible for largest cause of mortality in which the disease accounts for approximately 30% of the total cattle death worldwide and more than one billion dollars are annually lost in beef cattle industry(Boudreaux,2004) and in addition to the death losses, the cost of treatment is considerable (Radostits *et al*, 2007). Risk factors such as animal risk factor, environmental, managemental risk factor and the pathogen risk are involved in the complexity of the disease, as well as virulence factors including endotoxin, fimbrrae and leukotoxin are involved in the pathogenesis (Confer *et al*., 1990).

Generally, diagnosis relies on bacterial culture and specimen can be collected from the lower respiratory tract by tracheal swabs or bronchoalveolar lavage. Early recognition and treatment with antibiotics are essential for successful therapy. NSAID have been shown to be a beneficial ancillary therapy in treating bacterial pneumonia (Dalgleish, 1990). Vaccination regimes for respiratory pathogens should be completed at least 3 weeks before transportation and vaccine *M.haemolytica* which incorporate modified leucotoxin and surface antigen may produce production (Schreiber *et al.,* 2000). Therefore, the

objective of this paper is to give review on Epidemiology, Diagnosis, Prevention and Control of Pneumonic Pasteurellosis in cattle.

PNEUMONIC PASTEURELLOSIS

Definition

Pneumonic Pasteurellosis is a common disease of respiratory system of cattle as result of inflammation of pulmonary parenchyma which is usually accompanied by inflammation of bronchioles and often by pleurisy (Radiostits *et al.*, 1994).

Etiology

Pasteurella is a major cause of severe "shipping fever" pneumonia when combined with stress and with and without viral agents. The major bacterial pathogen involved in Pneumonic Pasteurellosis of cattle is *M.haemolytica* (*P.haemolytica* biotype A) serotype 1 (Radiostits *et al*., 1994; Hodgson *et al*., 2005). Eleven serotypes have been demonstrated within *M. haemolytica*, Serotypes 6, 2, 9 and 11 and untypable serotypes have been found in lesions of Pneumonic Pasteurellosis (Angen *et al*., 2002). *P. trehalosi* strains are commonly isolated causes and *P. multocida* biotype A occasionally (Brennan *et al*., 1997; Radiostits *et al*., 1994). The bacteria are Gram-negative, non-motile, non-spore forming, facultative anaerobic, small rods or coccobacilli (Holt *et al*., 1994).

Pasteurella and *Mannheimia* species can be distinguished by colonial, growth characteristics and by biochemical reaction, the strain of *P.multocida* can be differentiated by serotyping and serogroups can be identified on the basis of differences in capsular polysaccharides and are designated A, B, D, E and F. The organisms are further subdivided into about 16 somatic types on the basis of serological differences in the cell wall lipopolysaccharide. Serological methods for establishing both the capsular and somatic type include agglutination and agar jell diffusion test phenotypically, both *P.multicida* and *M.haemolytica* are similar with each other but unlike *P.multocida*, *M.haemolytica* do not ferment mannose (Quinn *et al*., 2002).

EPIDEMIOLOGY

Geographic Distribution and Occurrence

Pasteurellosis occurs worldwide but it is a particular problem in the tropics especially the hot, humid tropics where environmental stress is an important trigger mechanism of the disease complex (Seifert, 1996). It is a common disease of young growing cattle and common in America, the UK and North America. In Canada and the United states, the disease occurs most commonly in beef calves after

weaning in the fall of the year and is the most important disease in cattle that have been recently introduced into the feedlots (Radostits *et al*., 2007).

Method of Transmission

Transmission of pasteurellas probably occur by inhalation of infected droplet, coughed up or exhaled from infected animals which may be clinical case or recovered carriers in which the infection persists in the upper respiratory tract. *Mannheimia haemolytica* is carried in the nasopharynx and tonsils of apparently health animals where, interestingly, serotyping is most commonly isolated from cattle (Rowe *et al*., 2001).

Pasteurella multocida and *Mannheimia haemolytica* are highly susceptible to environment at influence and it is unlikely that mediated contagion is an important factor in the spread of the disease. When conditions are optimal, particularly when cattle are closely confined in inadequately ventilated trains or held for long periods in holding pens and feedlots, the disease may spread very quickly and affect high proportion of the herd within 48 hours (Radostits *et al*., 2007). Animal at pasture able to move freely and the rate of spread may be slower (Hall, 1994).

Morbidity and Mortality

Morbidity and mortality are affected by a number of factors and their interaction. Age, endemicity of the region, previous exposure and immunity are important factors. The high susceptibility of young animals has been established in several studies in Sri Lanka. Morbidity may reach 35%, the case fatality rate may range from 5-10%, and population mortality rate may vary from 0.75-1%. However, these morbidity and mortality may not be reliable because of wide variations in the method used to calculate disease incidence and prevalence (Radositis, *et al*., 2007). More recently in Britain, Morbidity rates of 73-100% with mortality of 0-8% of those affected and average mortality of 4% have been reported (Andrews**,** 2004).

Risk Factors

Animal Risk Factors

The disease occurs most commonly in young growing cattle from 6 months to 2 years of age, but all age groups are susceptible. Calves those are non-immune to *M.haemolytica* than calves that have serum neutralizing antibody to the organism and its cytotoxin. In western Canada auction market calves that originated from many different farms, and remixed at the market are at high risk. However, the distance that the calves were transported was not associated with fatal fibrinous pneumonia (Ribble *et al*., 1995).

Although the disease occurs most commonly in young beef cattle soon after their introduction to feedlot, it is not uncommon on dairy herd, especially when recent have been made. Mature beef cows are also

susceptible to Pneumonic Pasteurellosis if they are subjected to stress during the summer months or in the fall of the year. Usually associated with the movement of large groups to or from pasture during inclement weather herd outbreak of peracute pleuropneumonia due to *M.haemolytica* have been reported in adult dairy cattle *(*Harwood *et al.,* 1995*).*

Environmental and Managemental Risk Factors

Mixing of cattle from different source is an important risk factor, mixing of recently weaned beef calves from different source at auction market was associated with an increased risk of fatal fibrinopneumonia in calves moved to feedlot in a western Canada, especially in November shortly after action sales had peaked and when feedlot was reaching capacity (Ribble *et al*, 1995).

Stress is an intrinsic condition that was consistently reported to increase the susceptibility to various types of infectious disease. Stress can be induced artificially by administration of certain drugs and chemical compounds like dexamethasone (Zamri *et al*., 1991; Malazdrewich *et al*., 2004). Containment in dairy, humid and poorly ventilated barns, exposure to increment weathers, deprivation from feed and water are commonly followed by an outbreak of the disease in cattle. The reason for increased susceptibility to *M.haemolytica* infection in stressed animals was primarily attributed to the breakdown of innate pulmonary immune barriers by stressors (Martin, 1996).

Pathogen Risk Factors

The frequency of isolation of pasteurella species from the nasal passage of normal healthy unstressed calves is low but increased as animals are moved to auction market and then feedlot. The virulence factors of pasteurella species include fimbriae, polysaccharides, endotoxin and leucotoxins have been identified (Confer *et al*., 1990). Respiratory viruses were reported to impair the phagocytic function of pulmonary alveolar macrophage. An acute fatal respiratory disease was also induced in cattle by previous infection with Bovine herpes virus-1 challenged with *M.haemolytica* (Hodgson *et al*., 2005). *M.haemolytica* serotype A1 and A2 can survive for long period at time at least 156 days in bovine and tracheobronchial washings (Rowe *et al*., 2001).

Economic Importance

It is well established that Pneumonic Pasteurellosis is responsible for the largest cause mortality in feedlot animals in which the disease accounts for appropriately 30% of the total cattle death worldwide. The global economic impact of the disease is very well recognized and more than one billion dollars are annually cost in beef cattle industry (Boudreaux, 2004). In addition to the death losses, the cost of

treatment is considerable. It is also a disease of great importance in North America and Britain where it has caused great loss since before 1990s (Radositis *et al*., 2007).

Status of Pneumonic Pasteurellosis in cattle in Ethiopia

In a study under taken in calves with clinical signs of respiratory disease in the same area *M.haemolytica* and *P.multocida* isolates were obtained from nasal and transtracheal swabs (Tumeleasane, 2002). *M.haemolytica* serotype A_1 and A_2 are the most common in the country. However, no study has been done to know the prevalence and the actual organisms involved in Pneumonic Pasteurellosis of cattle (Adamsoun, 1990) but few studies have been done concerning Ovine Pneumonic Pasteurellosis in Central, North, Eastern, and South Eastern high lands of the country (Zeleke, 1998; Teferi, 2000; Sisay and Zerihun, 2003).

PATHOGENESIS AND VIRULENCE FACTORS

The pathogenesis of Pneumonic Pasteurellosis remained a subjective of considerable involved in the induction of speculation and controversy due to the complex nature of the disease and also factors Bovine Pneumonic Pasteurellosis were poorly defined (Yates *et al.*, 1982). However, the sequential development of the pulmonary lesion is highly mediated by complex interactions between the naturally existing causative organisms in the upper respiratory tract; the immunological status of the animal and the role of predisposing factors in the initiation of the infection. Under normal condition, the bovine lung is relatively treat pasteurellas because of an effective lung clearance mechanism. In other situation, the disease is essentially triggered by sudden exposure to stressful condition or by previous infection with Para influenza (PI-3) virus, Bovine herpes virus 1(BHV-1), and Bovine respiratory syntial virus (BRSV) that may predispose the bacterial incubation (Quinn *et al*., 2002).

The current hypothesis is that a combination of a viral infection of the respiratory tract and/or devitalizing influences from transportation, temporary starvation, weaning, rapid fluctuation in ambient temperature, the mixing of cattle from different origins and the excessive handling of cattle after arrival in a feedlot can all collectively promote an increase in the total numbers and virulence of pasteurella in the nasopharynx which are then inhaled into the alveoli and not effectively cleared (Radostitis *et al*., 1999).

Stress and viral infection would eventually impair the local pulmonary defense mechanism by causing deleterious effect on ciliating cells and mucous coating of the trachea, bronchi and bronchioles. The causative bacteria from the nasopharynx will then reach the central bronchi, bronchioles and alveoli by gravitation at drainage along the tracheal floor and there by become deeply introduced into the lung

tissue. Toxin produced by rapid growth and multiplication of the bacteria result in vascular disturbance and inflammatory reaction dominated by fibrinous exudates (Slocombe *et al*., 1985).

Four main virulence factors have been identified in strain of *M.haemolytica* and *P.trehalosi* (Confer *et al*., 1990). Fimbriae are small appendage, present in the surface of many gram-negative bacteria which enhance adherence to and colonization of the target epithelium of the susceptible animals. Two types of fimbriae have been detected in serotype 1 of *M.haemolytica* (Potter *et al.,* 1988; Merck *et al*., 1989). Both of them are capable of enhancing mucosal attachment of the organism and colonization of lower respiratory tract epithelium of cattle. Successful colonization will thus enable considerable increase in the number of bacteria needed in the lung tissue beyond the level that normal lung capacity could efficiently resolve (Gonzales and Maherswaran, 1993).

Similar to all other gram-negative bacteria the cell wall of *M.haemolytica* contains LPS endotoxin. This endotoxin is one of the most virulence factors involved in the pathogenesis of Pneumonic Pasteurollosis. It has been shown that serotypes 2 and 8 of *M.haemolytica* possess rough LPS while the other 14 serotypes have characteristic smooth LPS (Lacroix *et al*., 1993). Experimental evidence indicated that *M.haemolytica* endotoxin is directly toxic to endothelial cells and capable of altering leukocyte functions and causing lysis of blood platelets (Breider *et al*., 1990).

Leukotoxin is heat-labile protein, a pore-forming cytolysin that affects ruminant leukocytes and platelets and also considered as a main virulence factor for *M.haemolytica* (Zecchinon et *al*., 2005). The most susceptible cells are bovine macrophages, neutrophilis and lymphocytes. At low concentration, leukotoxin impairs phagocytosis and lymphocyte proliferation while at higher concentration it has cytotoxic effect resulting in cell death due to lysis. The polysaccharide capsule of the organism inhibits complement mediated serum killing as well as phagocytosis and intracellular killing of the organism. The capsules also enhance neutrophil-directed migration and adhesion of the organism to alveolar epithelium. The interactions of these virulence factors contribute to the pathogenesis of the disease (Jeyaseelan *et al*., 2002).

CLINICAL SIGNS

An observable clinical sign of respiratory distress usually develops within 10 to 14 days in adult mammals after being exposed to stress. Nevertheless, infected animals in severe cases may die as a result of toxemia even before the development of significant pulmonary lesions. In this case, Sudden death may be the first sign of acute out breaks, particularly in young calves (Radostits *et al*., 2007).

After the onset of respiratory disturbances, infected animals appear extremely dull with reduced appetite and remarkable depression. They soon develop high fever (40-41^{o}c or 104-106^{o}F) (Ackermann, 2000). Anorexia and rapid shallow respiration accompanied by mucopurulent nasal discharge. Later on, productive cough which is accentuated by physical effort or movement usually develop in most of the infected animals. In acute outbreak, the clinical course of the disease is relatively short (2-3 days) terminating in death or recovery in either treatment or non-treated animals. However, number of sick animals that survive the acute phase may become chronically infected animals. Marked dyspnea with an expiratory grunt may be observed in very advanced stages of disease (Dung Worth, 1993; Lopez, 2001).

DIAGNOSIS

Diagnosis is depending on the history of age, recent movement, weaning or housing, isolation and identification of the causative agent is important. Some of the livestock disease needed to be differentiated from the considered disease are; Contagious Bovine pleuropneumonia, Infectious Bovine Rhinotrachitis, Verminous pneumonia caused by Dictyocaulus viviparous and viral interstitial pneumonia (Hall, 1994).

Clinical Findings

The spectrum of clinical finding depends in part on whether the disease is occurring in groups of young cattle in large commercial feedlot, in small farm feedlot or in individual animals such as lactating dairy cows in which illness is earlier recognized by drop in milk production and feed intake. In the feedlot situation, affected animals must be identified primarily by visual observation followed by closer physical examination. However, close physical examination such as auscultation of the lungs have not been routinely used in feedlot, because of the time required to examine individual animals and the perceived accuracy of the examination in making clinical diagnosis (Radostits *et al*., 2007).

The relationship between clinical and pathological findings of disease in calves infected with *M.haemolytica* type A1 indicate that the respiratory rate, rectal temperature and clinical scores are significantly correlated with the extent of consolidation of the lungs. The respiratory rate increased from 30 per minute up to 70 per minute as the percentage of lung consolidation increased from 10% to 50%. The typical case of Pneumonic pasteurollosis reveals a fever (40-41^{o}C or 104-106^{o}F) (Ackermann, 2000). In early stages there are loud breathing sounds audible over the anterior and ventral part of the lung. Clinically when viewed from a distance, affected cattle are depressed and up on auscultation, rapid shallow respiration with loudness of breath sounds, nasal and ocular discharge are present (Radostits *et al*., 2007).

Laboratory Diagnosis

Microbiology cultures from the lower respiratory tract by tracheal swabs, transtracheal wash, or bronchoalveolar lavage are the most important laboratory diagnosis. Impression smears show bipolar staining organism with methylene blue. Examination or nasal swab sample from clinical case before treatment often yield bacteriological sample for pasteurella in which *M.haemolytica* biotype A serotype 1 is most common isolate obtained from cattle with Pneumonic Pasteurellosis (Quinn, 2002). *M.haemolytica* or *P.multocida* may be isolated from nasal swabs in live animals (Andrews, 2004).

Hematology of plasma fibrinogen concentrations are elevated paralleling the increase in body temperature and are reliable indication of the presence of the lesion. Young cattle with clinical signs of acute respiratory disease, a fibrinogen concentration is greater than 0.7g/dl and temperature greater than 40^{o}C (104^{o}F) are likely to have Pneumonic Pasteurellosis. Acute phase proteins are increased within 24 hours following experimental intratracheal inoculation of *M.haemolytica* into calves. The availability of rapid test for acute phase protein could assist in the field diagnosis of the disease and its possible determination from similar disease (Radostits *et al*., 2007). Serology and mere isolation of P. multocida from nasal swabs is of little value without being able to predict pathogenicity. The application of the polymerase chain reaction (PCR) to detect and differentiate toxin producing and nontoxin producing P. multocida may prove to be a useful technique for control of both pneumonic pasteurellosis and atrophic rhinitis (Patrick, 2015).

Necropsy Findings

There is marked pulmonary consolidation, usually involving at least the antero-ventral part of the lungs. The lung is firm, and the cut surface usually reveals an irregular, variegated pattern of red, white, and gray tissue due to hemorrhage and necrosis. Occasionally sequestrate of necrotic lung tissue are found. *P.multicoda* cause fibrino-purulent bronchopneumonia without the multifocal coagulation hemolytic necrosis that characteristics of fibrinous lobar pneumonia associated with *M.haemolytic*a (Daoust, 1989). The post mortem findings of lung consolidation and pleurisy are present. The basic post mortem lesions are acute fibrinohemorrhagic pneumonia with pleuritic adhesion (Andrews, 2004).

TREATMENT, PREVENTION AND CONTROL

Treatment

Treatment should begin early. Most cattle will show some improvement within one to three days of initiating treatment. Broad spectrum antibiotics are used commonly. Antibiotics most commonly used are oxytetracycline at rate 20mg/kg BW, IM, long acting and 10mg/kg daily for 3 days short acting;

Tilmicosin at rate 10mg/kg BW, SC and repeat 72hr later if necessary; florfenicol (analog of thiamphenicol) 20mg/kg BW, IM repeat 48 hr and mass medication with sultomethazine 100mg/kg BW in drinking water for 5-7 days. Tilmicosin is effective in reducing the population of *M.haemolytica* that colonizing the nasal cavities of calves with respiratory disease (Frank and Duff, 2000).

Studies in Canada showed that oxytetracycline was usually the antimicrobial drug of first choice for treating case of shipping fever (Martin *et al*., 1983). Florfenical given on arrival reduce the incidence of respiratory diseases and reduce the colonization of nasopharynx by *M.haemolytica* (Frank and Briggs, 2002). If pulmonary abscessation has occurred, it is difficult to achieve resolution with antimicrobials and culling of animal should be considered. NSAIDS have been shown to be a beneficial ancillary therapy in treating bacterial pneumonia (Dalgleish, 1990).

Prevention and Control

Whilst it has now been accepted that pasteurellus species are the primary cause of Pneumonic Pasteurellosis, nevertheless viral infections and stress such as transport, new environment and mixing with new animals are important factors that predispose calves to the disease. Consequently, in the UK, the disease is primarily a problem in beef fattening units, particularly in those where weaned calves are bought from other farms via cattle market. Prevention and control of Pneumonic Pasteurollosis has centered on the predisposing factors in combination with vaccination and management where herds are at high risk (Quinn, *et al.*, 2002).

Management Strategies

Because of common occurrence of the disease at the time of shipment from the range to the feedlot, much attention has been given to reduce the incidence of disease at this time. The calves should be transported from the farm of origin directly to the fattening unit. The transport distance should be as short as possible and the animal should be handled in calm and considerate manners at all stages of transport. The calves could wean and introduced to fattening diet at least two weeks before leaving farm (Radostits *et al*., 2007).

Vaccination

Pasteurella vaccines and respiratory viral vaccines have been used extensively in an attempt to control Pneumonic Pasteurellosis in cattle. However, their efficacy appeared to be low and literature review suggest that at present there is little evidence to show efficacy of such vaccines under feedlot conditions .Vaccination regimes for respiratory pathogens should be completed at least 3 weeks before transportation and vaccine for *M.haemolytica* incorporate modified leukotoxin and surface antigen induce production

(Schrever *et al*, 2000). The experimental lung challenge of calves with formalin killed *P.multocida* does not provide subsequent protection to challenge with live *P.multicida* (Dowling *et al*., 2004).

Single vaccination of a *M.haemolytica* bacterin toxoid given to calves on arrival in the feedlot reduced overall mortality. Vaccination of calves after arrival in the feedlot with genetically attenuated leucotoxin *M.haemolytica* combined with its extracts reduced morbidity due to bovine respiratory disease. Several outer membrane protein of *P.multocida* type A3, which occasionally causes severe bronchopneumonia in cattle, may be important for immunity for organism (Thorlacson *et al*., 1990). Vaccination of colostrum-deprived calves at 2 and 4 weeks 0f age with a *M.haemolytica*, a culture supernatant vaccine resulted in high titer of IgA antibody to capsular polysaccharides within one week of vaccination (Hodgsons, 2000).

Chemoprophylaxis

Chemoprophylactic measures for preventing Pneumonic Pasteurellosis are useful for preventing the outbreak of the disease, especially when disease provoking stress is consciously put up with. Application of long acting oxtetracycline before shipping animals over a long distance will protect the animals effectively against shipping fever. The Antibiotic chemoprophylaxis of Pasteurellosis is the only way to stop the infection immediately during a sudden outbreak and prevents its spreading to other animals or herd. In such cases, the chemoprophylaxis replaces the application of hyperimmune serum which used to be applied, (Seifert, 1996). Generally, the use of good management practices and a strategic vaccination program to prevent Pneumonic Pasteurellosis is much preferable to the treatment. Although generally considered to be effective, the prophylactic use of antibiotics has raised public health concerns with the food animal industry coming under increasing pressure to limit the use of antibiotic (Radostits *et, al*, 1994).

CONCLUSION AND RECOMMENDATIONS

Pneumonic Pasteurellosis is a common disease of respiratory system of cattle as result of inflammation of pulmonary parenchyma which is usually accompanied by inflammation of bronchioles and often by pleurisy. The disease primarily results from interaction of strain, immunity and the causative bacteria (*M.haemolytica*) which is commensally resident in respiratory tract of susceptible animals. There are multiple stresses that precipitate the disease.

The disease is distributed worldwide, and mostly transmitted by inhalation from infected droplets. The most important virulence factors involved in the pathogenesis are fimbriae, polysaccharide capsule, endotoxin and leukotoxin. Diagnosis is depending on the history of age, recent movement, weaning or housing, isolation and identification of the causative agent is important. Effective control is based on management, vaccination and chemoprophylaxis.

Based on the above conclusion, the following recommendations are forwarded.

- Avoid overcrowding of cattle at a time of transportation to feedlot.
- Providing a prophylaxis drug during loading of animals in case of transportation.
- The calves should be weaned and introduced to fattening diet at least two weeks before leaving farm.
- Infected animals should be isolated and treated early.
- Emphasis should be on improved management system.
- Vaccination of animal at least 3 weeks before transportation.
- Further research has to be conducted on the status of Pneumonic Pasteurellosis in cattle in Ethiopia.

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